

Conclusion: 5-LO expression is induced by RSG and depends on PPAR γ activation in astrocytes. RSG-induced 5-LO activity is necessary for neuroprotection and leads to LXA₄ synthesis, which then activates PPAR γ in astrocytes. These results strongly suggest a novel mechanism of action of RSG, through late PPAR γ activation by potent anti-inflammatory compounds like LXA₄.

PS3-09

t-PA treatment induces an increment of circulating endothelial progenitor cells in human ischemic stroke

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Introduction: Tissue plasminogen activator (t-PA) is an effective treatment for acute ischemic stroke. Likewise, tPA treatment leads to an increase in the levels of MMP-9, which is a potent stimulator of the increment of circulating EPCs. Similarly, EPC proliferation is mediated by other molecular mechanisms as VEGF or SDF-1 α . As neovascularization may be a therapeutic target in cerebral ischemia, our aim was to study the influence of t-PA treatment in the EPC increment after acute ischemic stroke.

Patients and Methods: Forty-eight patients [24 males, average 70.7 (10) years] with first ever non-lacunar ischemic stroke (< 12 h from onset) were prospectively studied. Fifteen patients were treated with t-PA within 3 h from symptom onset following the SITS-MOST criteria. EPC colonies were quantified as early outgrowth colony forming unit-endothelial cell (CFU-EC). CFU-EC were calculated at admission (previous to tPA treatment) day 7 (1), and at 3 months (7) days. We defined the increment of EPC colonies during the first week as the difference in the number of CFU-EC between day 7 and admission. Serum levels of VEGF, SDF-1 α and active MMP-9 were measured by ELISA on admission, at 24 and 72 h, day 7, and 3 months.

Results: CFU-EC were similar at baseline between patients treated and non-treated with t-PA [8.8 (6.8) vs. 8.3 (4.5) CFU-EC, $P=0.815$]. Patients treated with t-PA showed a higher CFU-EC absolute increment during the first week [33.1 (17.9) vs. 2.4 (10.6) CFU-EC, $P<0.0001$]. In the multivariate analyses, t-PA treatment was independently associated with EPC increment (B : 26.5; IC 95%: 9.3-33.7; $P<0.0001$). Besides, patients treated with t-PA showed higher levels of VEGF at 24 and 72 h, SDF-1 α and active MMP-9 at 24 h.

Conclusion: These findings demonstrate the association between tPA treatment and EPC increment. Fibrinolysis, probably by an increment of molecular factors such as VEGF, MMP-9 and SDF-1 α , plays an important role in the increase in the number of EPCs in acute ischemic stroke.

PS3-10

Protective role of LXR receptor in experimental stroke **MORALES J.R.,* HURTADO O.,* VIVANCOS J.,* NOMBELA F.,* CASTRILLO A.,† LIZASOAIN I.* and MORO M.A.***

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Introduction: Liver X receptors α (LXR α) and β (LXR β) are ligand-activated transcription factors that belong to the superfamily of nuclear receptors. Apart from their role in the regulation of cholesterol homeostasis and fatty acid metabolism, LXR receptors have been described to inhibit the expression of several inflammatory mediators. As these anti-inflammatory actions might be useful in stroke, we have investigated the effects of the LXR agonists GW3965 and T0901317 on stroke outcome in a rodent model of cerebral ischaemia.

Methods: Male Fischer rats were used. Infarct size: 48 after MCAO, animals were sacrificed and a serial of 2 mm thick coronal slices were made and stained. Infarct size was determined using a computer image analysis system. Experimental groups were control, permanent middle cerebral artery occlusion (MCAO), MCAO + GW3965 (20 mg/kg) MCAO + T0901317 (20 mg/kg) or vehicle (DMSO). Protein expression of iNOS, COX-2 and MMP9 in cerebral cortex were studied by Western blot. Cytokine levels were determined by EIA.

Results: Administration of GW3965 (20 and 50 mg/kg) or T0901317 (20 and 50 mg/kg) 10 min after the occlusion caused a decrease in MCAO-induced infarct size about 20% vs. MCAO. Furthermore, GW3965 reduced MCAO-induced expression of iNOS ($41 \pm 1\%$ of MCAO, $n=4$, $P<0.05$), COX-2 ($43 \pm 3\%$ of MCAO, $n=4$, $P<0.05$) and MMP-9 ($43 \pm 1\%$ of MCAO, $n=4$, $P<0.05$). LXR agonists also reduced IL-1 β levels when compared with the MCAO group ($68 \pm 2\%$ of MCAO), but TNF- α levels were not affected.

Conclusions: Activation of LXR by specific agonists cause neuroprotection after experimental stroke, mainly by anti-inflammatory mechanisms.

PS3-11

High serum levels of endothelin-1 are associated with cerebral edema in patients with acute ischemic stroke treated with t-PA

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Introduction: Endothelin-1 (ET-1) is a powerful vasoactive peptide secreted by the endothelial cells. It mediates different effects depending on its cellular receptor: receptor A mediates vasoconstriction and receptor B mediates vasodilatation, and it is possible that ET-1 could mediate development of cerebral edema. Cerebral edema is associated with poor outcome in